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(54) Title: SOLID PRODUCTS AND METHODS FOR THE REMINERALIZATION AND PREVENTION OF DEMINERALIZATION OF TEETH		
(57) Abstract <p>Solid products for remineralizing subsurface lesions and/or mineralizing exposed tubules in dentin containing an anionic component composed of at least one phosphate salt and a cationic component composed of at least one calcium salt. The cationic components and the anionic components are mixed in a carrier component and then coated on an insoluble, solid substrate. Subsurface lesions and/or exposed dentin tubules in a tooth are remineralized by the rapid and simultaneous release of the calcium and phosphate salts into water and/or saliva such that the subsurface lesions and dentin tubules are permeated by the calcium and phosphate ions. The calcium and phosphate ions precipitate as water-insoluble calcium phosphate in the subsurface lesions or dentin tubules. The products may be in the form of dental floss, tooth picks, dental adhesives, and implants.</p>		

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SOLID PRODUCTS AND METHODS
FOR THE REMINERALIZATION AND PREVENTION OF
DEMINERALIZATION OF TEETH

BACKGROUND OF THE INVENTION

The present invention relates to improved solid products and methods for remineralizing subsurface lesions in teeth and for mineralizing exposed tubules in dentin to prevent demineralization thereof. More particularly, the present invention relates to solid products having a solid substrate containing remineralization salts such as calcium salts and phosphate salts to be applied to lesions in dental enamel to remineralize the lesions in teeth and/or to mineralize exposed tubules in dentin, and to methods of using such solid products.

The primary component of enamel and dentin in teeth is calcium phosphate in the form of calcium hydroxyapatite. While highly insoluble at normal oral pHs, the calcium phosphate in the teeth tends to be relatively soluble in acidic media. Consequently, carious lesions can form in the subsurface of a tooth when such tooth is exposed to acids formed from the glycolysis of sugars caused by various oral bacteria.

Because saliva is supersaturated with respect to calcium and phosphate ions, saliva helps protect teeth against demineralization and can slowly remineralize teeth which have become demineralized by acids. It is well known that the presence of fluoride ions can enhance the natural remineralization process and this is one of the accepted mechanisms by which fluoride toothpastes and rinses protect against caries. However, the efficacy of fluoride-containing toothpastes and rinses to

remineralize teeth is limited by the modest levels of calcium and phosphate in saliva. It is evident from the art that it is highly desirable to increase the available concentration of calcium and phosphate ions in the oral cavity to speed up the remineralization process. However, because of calcium phosphate's low solubility at the pH of saliva, the addition of higher levels of dissolved calcium and phosphate ions is not easily accomplished.

Remineralization of dental enamel has been carried out experimentally, both in vivo and in vitro. Some studies have concentrated on the remineralizing properties of saliva and of synthetic solutions supersaturated with respect to hydroxyapatite. Such studies comprise the subject matter of U.S. Patent Nos. 3,679,360 (Rubin) and 4,097,935 (Jarcho).

The supersaturated solutions or slurries used in the aforementioned Rubin and Jarcho patents for remineralization experiments have been prepared from a single form of calcium phosphate. When a carious lesion is flooded with one of these supersaturated solutions, the calcium and phosphate ions in the form of precipitated hydroxyapatite remineralize the lesion. However, use of these solutions is impractical for several reasons. First, the amount of calcium and phosphate ions available for remineralization in these supersaturated solutions is too low. It is reported that it takes approximately 10,000 unit volumes of the usual supersaturated solution to produce one unit volume of mineral. Thus, remineralization by this method requires both an excessive volume of fluid and an excessive number of applications. The supersaturated solutions are inherently limited in this respect because such solutions

cannot maintain their supersaturated state. When the hydroxyapatite precipitates out to the point where the solution is no longer supersaturated, a new supersaturated solution must be introduced or the
5 remineralization process stops.

Another problem with single calcium phosphate slurries is that as the hydroxyapatite precipitates out of solution, the pH of the solution changes. Unless the old solution is removed from contact with the tooth
10 material, the solution may become too acidic or alkaline and may damage the dental tissue.

U.S. Patent No. 4,080,440 (DiGiulio et al) discloses a metastable solution of calcium and phosphate ions at a low pH (between 2.5 and 4.0) under which
15 conditions the solubility of calcium phosphate salts is high. After penetration of the solution into demineralized enamel, remineralization results from the precipitation of calcium phosphate salts when the pH rises. Fluoride ions can be included in the metastable
20 solution. A significant disadvantage of the use of metastable solutions is that the relatively low pH might demineralize the dental enamel and/or injure other tissue.

U.S. Patent Nos. 4,177,258, 4,183,915 and
25 4,348,381 (Gaffar et al) disclose a remineralizing solution containing supersaturated concentrations of calcium ions, phosphate ions and a fluoride source stabilized by the presence of an antinucleating agent such as diamine tetramethylenephosphonic acid,
30 ethylenediamine tetramethylenephosphonic acid and 2-phosphonobutane-tricarboxylic acid-1,2,4, or the water-soluble salts thereof. This solution is preferably adjusted to the neutral pH range where the solution is

alleged to most effectively remineralize sub-surface lesions. Even though the antinucleating agent would be expected to stabilize the solution, equilibrium of the supersaturated concentrations is still found difficult to
5 maintain and avoid precipitation of hydroxyapatite and changes in the pH of the solution. Most importantly, in order to obtain long-term storage stability of these solutions, the concentration of calcium phosphate and, if used, fluoride is severely limited, thus limiting the
10 remineralization potential of the formulation.

U.S. Patent Nos. 4,083,955 (Grabenstetter et al) and 4,397,837 (Raaf et al) disclose a process for remineralizing demineralized enamel by the consecutive treatment of tooth surfaces with separate solutions
15 containing calcium ions and phosphate ions. In this process, fluoride ions may be present in the phosphate solutions. It is immaterial which ionic solution is used to treat the teeth first. By sequentially applying calcium and phosphate ions to the tooth surface, high
20 concentrations of the ions are able to penetrate into lesions in solution form, where the ions precipitate as a calcium phosphate salt when ions from the second treatment solution diffuse in. While apparently successful, this method involves the inconvenience of a
25 plurality of sequential applications which can be time consuming.

U.S. Patent No. 4,606,912 (Rudy et al) teaches a method of making a clear aqueous mouthwash solution capable of remineralizing lesions in teeth by forming an
30 aqueous solution containing a source of calcium ions and a chelating agent for calcium ions, causing the chelation of at least 50% of the calcium ions and subsequently adding a source of phosphate ions to the aqueous

solution. Here too, while somewhat effective, the addition and necessary control of the amount of chelating agent makes the concept impractical.

Another problem with known remineralization techniques is that the remineralization may stop before the lesion is completely remineralized due to build-up of the remineralized tooth material in or on the outer layer of the tooth's surface. This build-up occurs when the rate of remineralization is too fast and prevents the diffusion of the mineral into the deeper regions of the lesion, thus thwarting the full remineralization of the tooth.

U.S. Patent Nos. 5,037,639; 5,268,167; 5,437,857; 5,427,768; and 5,460,803 (all to Tung) involve the use of amorphous calcium compounds such as amorphous calcium phosphate (ACP), amorphous calcium phosphate fluoride (ACPF) and amorphous calcium carbonate phosphate (ACCP) for use in remineralizing teeth. These amorphous compounds or solutions which form the amorphous compounds when applied either onto or into dental tissue prevent and/or repair dental weaknesses such as dental caries, exposed roots and dentin sensitivity. The compounds are claimed to have high solubilities, fast formation rates and fast conversion rates (to apatite).

Remineralization is accomplished by bringing the amorphous compound into contact with the dental tissue. This can be done directly, i.e., putting an amorphous compound directly on the tooth, or indirectly through a carrier, i.e., incorporating the amorphous compound in a carrier such as a gel, a chewing gum, or a toothpaste and applying the carrier to the dental tissue. Once contact is established with the tooth, the amorphous calcium phosphate compounds will recrystallize to the

less soluble apatite form in the lesion and reform the tooth. However, under conditions where amorphous calcium phosphate compounds are stable, the quantity of calcium and phosphate released is relatively low and, therefore,
5 remineralization is slower than desirable.

The aforementioned patents to Tung also teach the use of two-part solutions wherein a first part contains phosphate salt(s) and a second part contains calcium salt(s), wherein either the first part or the
10 second part further contains carbonate salt(s). In addition, the Tung patents teach solutions formed by dissolving in water a solid powder containing calcium salt(s), phosphate salt(s), and carbonate salt(s). These solutions are then applied to dental tissue. The Tung
15 patents further teach the use of non-carbonated solid powders containing mixtures of calcium salts and phosphate salts which can be applied directly to the tooth or dispersed in gel, chewing gum, or other non-aqueous mediums such as toothpaste which is placed in
20 contact with the tooth. The patents teach that these powders are easily dissolved in saliva and then reprecipitated as an amorphous calcium phosphate compound. However, the Tung patents do not disclose the pHs of aqueous solutions formed from the non-carbonated
25 solid powder.

Effective remineralizing/mineralizing products and methods are continually desired which do not require the presence of carbonate salts to achieve stability, remineralization and/or mineralization. It is also
30 continually desirable to provide remineralizing/mineralizing products and methods which directly form hydroxyapatite at the subsurface of the tooth rather than first forming an amorphous calcium

phosphate as an intermediate. In addition, it is continually desirable to provide a remineralization product in the form of a one-part, stable remineralizing composition which is not negatively affected by a rise in
5 pH or temperatures or which can efficiently remineralize teeth. Finally, there is a continual need for a method of remineralizing dental enamel which employs a stable, one-part remineralizing product which does not require excessive amounts of calcium and phosphate salts or
10 inordinately long, frequent or sequential exposure times.

Remineralizing/mineralizing one-part and two-part products which overcome many of the aforementioned problems are disclosed in commonly assigned U.S. Patents 5,603,922; 5,605,675; 5,645,853; and 5,571,502.

15 U.S. 5,603,922 discloses one-part and two-part products and methods of using same to remineralize subsurface lesions. The one-part and two-part products contain at least one water-soluble calcium salt, at least one water-soluble divalent metal salt wherein the
20 divalent metal is other than calcium and at least one water-soluble phosphate salt. In the two-part products, the calcium and divalent metal salts are disposed in a first discrete component, and the phosphate salt(s) is disposed in a second discrete component. The two-part
25 product may further contain a dispensing means for allowing the first and second components to be simultaneously dispensed from the product to permit the dispensed first and second components to simultaneously contact the tooth or teeth being treated. The aqueous
30 solution formed by mixing the salts used in the one-part and two-part products has a pH of from about 4.0 to about 7.0.

U.S. 5,605,675 discloses a two-part product and method of using same for remineralizing dental enamel, wherein the product contains a first discrete component containing at least one water-soluble calcium salt and a
5 second discrete component containing at least one water-soluble phosphate salt and at least one water-soluble fluoride salt. The product may further contain a means for allowing the first and second components to be simultaneously dispensed from the product. The first and
10 second components of the product each have a pH such that when the two components are mixed to form an aqueous mixed solution, the solution has a pH of from about 4.5 to about 10.0.

U.S. 5,645,853 is directed to a chewing gum
15 product and method of using same for remineralizing subsurface lesions in teeth, wherein the product contains a water-soluble cationic portion composed of at least one water-soluble calcium salt and at least one water-soluble, non-toxic divalent metal salt wherein the
20 divalent metal is other than calcium; a water-soluble anionic portion containing at least one water-soluble phosphate salt; and a gum base. The anionic and cationic portions are disposed in the product such that chewing of the product in the presence of water and/or saliva causes
25 the anionic and cationic portions to be simultaneously released into the water and/or saliva to form a mixed aqueous solution therewith. The anionic and cationic portions each have a pH when dissolved in water and/or saliva such that the mixed aqueous solution has a pH of
30 from about 4.0 to 7.0.

U.S. 5,571,502 is directed to one-part, non-aqueous products and methods of using same for remineralizing subsurface lesions, wherein the products

contain at least one water-soluble calcium salt; at least one water-soluble phosphate salt; either a stabilizer or a hydrophilic, non-aqueous, water-soluble vehicle; and, optionally, at least one water-soluble fluoride salt.

- 5 When the components are mixed with water or saliva to form an aqueous mixed solution, the solution has a pH of from about 4.5 to about 10.0.

In the products disclosed in the foregoing commonly assigned patents, the cationic and anionic
10 components are kept separate from one another until use of the product. In addition, the cations and anions are delivered simultaneously to the surface of the tooth being treated. These factors, along with the pH of the aqueous solution and the use in some cases of at least
15 one water-soluble divalent metal salt, are helpful to allowing the cations and anions to have ample time to diffuse through the surface of the tooth to the subsurface before undergoing precipitation.

For mineralization or remineralization of
20 enamel or dentin to occur, the concentration of calcium and phosphate ions in saliva must be above the concentration required to saturate the solution with respect to the formation of calcium hydroxyapatite, octacalcium phosphate, dicalcium phosphate dihydrate, or
25 other forms of insoluble calcium phosphate. At pHs above about 6.5, these requirements are met by the levels of calcium and phosphate in normal human saliva. However, because the concentration of calcium and phosphate ions in normal human saliva is only modest, even at pHs above
30 6.5, the rate of mineralization produced by normal saliva is very slow even when fluoride is present to catalyze the process. When the pH is above about 7, raising the concentration of calcium and phosphate ions much beyond

that normally present in saliva does not, however, significantly increase remineralization. Because of the high insolubility of calcium phosphate salts above pHs of about 7, excessively rapid precipitation occurs which
5 does not allow time for the ions to penetrate the tooth.

At pHs below about 7, significant remineralization will occur only if the concentration of calcium and phosphate ions in the saliva is above the concentration required to saturate the solution with
10 respect to the formation of dicalcium phosphate dihydrate. Under these pH conditions, it has been demonstrated that remineralization can be accelerated by increasing the degree of supersaturation in saliva. Inasmuch as the solubility of dicalcium phosphate
15 increases with decreasing pH, it has been found that when lesions are remineralized with solutions having a pH in the range of 4.5 to 7.0 and containing supersaturated quantities of calcium and phosphate ions, the optimum concentration of calcium ions needed to maximize the
20 process increases with decreasing pH. Below a pH of about 4.0, dicalcium phosphate dihydrate becomes the stable precipitating species from supersaturated solutions. Under these pH conditions, it takes very high levels of calcium and phosphate to saturate the
25 solutions. Under such conditions, there is a real danger with fairly high concentrations of calcium and phosphate that the solution will be undersaturated and demineralization of the teeth being treated will occur.

It has also been found that the simultaneous
30 provision of very high calcium and phosphate ion concentrations can result in premature precipitation of the calcium salt before the ions can penetrate the tooth

or premature precipitation which blocks the entrances of the pores in tooth enamel and dentin and thereby prevent further remineralization.

Thus, a problem apparently exists in that to
5 control untimely precipitation, the concentration of either the dissolved calcium ions or the dissolved phosphate ions needs to be limited. This in turn would be expected to disadvantageously limit the maximum rate of mineralization or remineralization which could be
10 accomplished. Thus, there is a need to prevent untimely precipitation of calcium and phosphate ions and simultaneously maximize mineralization or remineralization.

The remineralization products disclosed in the
15 aforementioned commonly assigned patents are very effective for remineralizing teeth. However, it is desirable to provide alternative products which minimize the risk of premature precipitation of calcium phosphate as well as to optimize remineralization of subsurface
20 lesions in teeth.

In addition to a product that controls the untimely precipitation of calcium and phosphate salts, it is also highly desirable for a remineralization product to release remineralization salts over an extended period
25 of time especially in the interproximal surfaces of teeth where food particles and bacteria can lodge to cause the formation of dental caries.

U.S. Patent No. 4,638,823 discloses a fluoride-coated dental floss which claims to have enhanced
30 bactericidal activity. Stannous fluoride is coated on dental floss in a mixture of water-soluble wax such as

polyethylene glycol. The fluoride is deposited on interproximal teeth surfaces during flossing to prevent bacterial growth.

U.S. Patent No. 4,414,990 also discloses a
5 fluoride-coated dental product. The fluoride is coated on the dental floss in a polymeric coating in contrast to a wax coating. The polymeric coating is water soluble. During flossing the polymeric coating dissolves releasing the fluoride into the interproximal spaces and
10 subgingival surfaces of teeth to hinder bacterial growth.

Although there are solid products for depositing fluoride onto teeth to hinder bacterial growth to prevent the formation of dental caries, such solid products do not provide for the release of calcium and
15 phosphate salts into the of teeth for the remineralization of teeth or the mineralization of dentin tubules.

Accordingly, a primary object of the present invention is to provide solid products and methods for
20 the remineralization and the prevention of demineralization of human teeth, where the solid products and methods are capable of effectively incorporating calcium ions, phosphate ions and, if present, fluoride ions into the subsurface of a tooth.

25 A further object of the present invention is to provide products and methods for the remineralization and the prevention of demineralization of human teeth, where the precipitation of the calcium, phosphate and, if present, fluoride ions is substantially avoided prior to
30 diffusion of the ions into the subsurface of a tooth without reducing the rate of remineralization at the subsurface of the tooth.

Still another object of the present invention is to provide solid products for the remineralization and the prevention of demineralization of human teeth, wherein the solid products are easily usable by the consumer and do not differ significantly, in flavor or appearance, from customary dental cosmetics.

Yet another object of the present invention is to provide an improved solid product and a method of preparing such solid product, where the solid product is maintainable in a single container, substrate or matrix and is capable of remineralizing lesions in the teeth and mineralizing normal teeth to prevent cariogenic lesions from forming therein.

A further object of the present invention is to provide remineralizing/mineralizing solid products and methods which can directly form hydroxyapatite in the subsurface of a tooth subsurface without first forming an amorphous calcium phosphate as an intermediate.

A further object of the present invention is to provide for products and methods for the extended release of remineralization salts into the interproximal and subgingival surfaces of teeth to prevent dental caries.

These and other objects which are achieved according to the present invention can be readily discerned from the following description.

SUMMARY OF THE INVENTION

The present invention provides effective remineralizing/mineralizing solid products and methods of using same which overcome the aforementioned problems and achieve the foregoing objects.

The present invention provides solid products for remineralizing subsurface lesions and/or mineralizing

exposed dentin tubules in teeth, containing:

(a) a cationic component comprising at least one calcium salt;

(b) an anionic component comprising at least
5 one phosphate salt;

(c) a carrier component for retaining parts (a) and (b) in the product such that parts (a) and (b) do not react prematurely; and

(d) a solid substrate onto which components
10 (a), (b) and (c) adhere to a surface of the solid substrate; the solid product is capable of simultaneously releasing the components of part (a) and the components of part (b) from (c) the carrier component into water and/or saliva when the product is contacted or mixed with
15 the water and/or saliva.

Remineralization and/or mineralization is effected by contacting or mixing the above-described solid product with water and/or saliva such that the solid product releases components (a) and (b) from
20 carrier component (c) into the water and/or saliva to form a mixed aqueous composition, and then applying the mixed aqueous composition to at least one surface of at least one tooth for a period of time sufficient to allow the dissolved calcium cations and the dissolved phosphate
25 anions to diffuse through the surface of the tooth to the subsurface and/or onto or into the dentin tubules, wherein the diffused cations and anions precipitate to form an insoluble compound on the subsurface lesion and/or onto or into the exposed dentin tubules, thereby
30 remineralizing such lesion and/or mineralizing such exposed tubules.

When the mixed aqueous composition is applied to the tooth (or teeth), the dissolved calcium cations and the dissolved phosphate anions in the aqueous composition do not immediately precipitate but rather
5 diffuse through the surface of the tooth to the subsurface and/or onto or into dentin tubules thereof, where the ions then precipitate to form an insoluble compound on the demineralized subsurface lesion(s) and/or onto or into the exposed dentin tubule(s).

10 The solid products of the present invention also permit the placement of the remineralization salts at specific sites on a tooth or teeth that are especially susceptible to the formation of dental caries such as on the interproximal surfaces, at places close to the gum
15 line or the subgingival surfaces where many periodontopathogens and cariogenic bacteria reside. In addition, the solid products of the present invention may assist in removing plaque and entrapped food particles helping to reduce the formation of dental caries, the
20 tendency toward gingivitis and mouth odor as well as generally improving oral hygiene.

Additionally, by depositing the remineralization salts such as calcium and phosphate ions at specific sites on a tooth, the solid products of the
25 present invention provide for an extended release of remineralization salts at sites which may be especially susceptible to the formation of dental caries.

Thus, the solid products of the present invention provide for a means for remineralizing teeth
30 and/or mineralizing dentin tubules at desired specific sites and at the same time provide an extended release of calcium and phosphate salts from the solid product.

In addition, the methods of the present invention overcome the disadvantages of the methods discussed hereinabove in that the methods of this invention effect subsurface remineralization rather than surface remineralization. Since dental caries often begins as a subsurface demineralization of the dental enamel, subsurface remineralization arrests and repairs the carious lesion before any permanent structural damage to the tooth occurs.

Furthermore, the methods of the present invention do not require preparation of the enamel surface, capping of the tooth, or removal of decay products.

In addition, consumers may conveniently practice the methods of the present invention without substantially changing their dental care habits.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed to solid products and methods of using same to remineralize subsurface lesions in teeth and/or to mineralize exposed tubules in dentin.

As used herein, the term "solid product" refers to a product having a hard consistency and which can be placed in the oral cavity. Non-limiting examples of solid products within the scope of the present invention include, but are not limited to dental floss, dental tape, tooth picks, dental adhesives, implants and the like.

The solid products of the present invention contain (a) a cationic component of at least one calcium salt; (b) an anionic component of at least one phosphate salt; (c) a carrier component for retaining part (a) and

part (b) in the product such that the components of parts (a) and (b) do not prematurely react and (d) a solid substrate onto which components (a), (b) and (c) adhere to a surface of the solid substrate. The cationic (a) and the anionic (b) components are preferably rapidly and simultaneously released into water and/or saliva such that the calcium and phosphate salts penetrate the subsurface of tooth enamel and dentin tubules before the precipitation of water-insoluble calcium phosphate to remineralize subsurface lesions and/or mineralize exposed dentin tubules in teeth. Thus, the solid products of the present invention provides for water soluble or partially water soluble calcium and phosphate ions such that the ions penetrate the subsurface of tooth enamel and dentin tubules without an untimely precipitation of calcium phosphate.

Additionally, the solid products advantageously provide for a means of depositing the remineralization salts at or near specific sites on a tooth (teeth) where mineralization or remineralization may be especially needed. For example, the solid products can readily deposit remineralization salts for extended release on the interproximal surfaces, at places close to the gum line or on the subgingival surfaces of teeth where periodontopathogens in combination with cariogenic bacteria may thrive and cause dental caries. Such surfaces of teeth are difficult to clean thus prone to the formation of cavities.

The components (a) and (b) have a pH in water such that a mixed aqueous composition formed by mixing components (a) and (b) with water and/or saliva has a pH of from about 4.0 to about 10.0. Preferably, the pH is from about 4.5 to about 6.5, and most preferably from

about 5.00 to about 5.75. At a pH within such ranges, high concentrations of the calcium cations, and phosphate anions in the mixed aqueous composition remain soluble for a period of time sufficient to allow the ions to
5 diffuse through the surface of the tooth to the subsurface of the enamel and/or on the dentin thereof.

If the mixed aqueous composition has a pH below about 3, demineralizing will occur rapidly. A pH below about 2.5 is undesirable from a safety standpoint. Such
10 acidic pHs can damage or irritate the tissue of the oral cavity. Thus, components (a) and (b) of the products form a pH in water and/or saliva such that the mixed aqueous composition formed therefrom has a pH within the aforementioned ranges.

15 In products of the present invention at least one or more water-soluble salt of a divalent metal other than calcium may be included. In addition, the products may further contain at least one water-soluble fluoride salt.

20 As used herein, the term "water-soluble" with respect to the calcium salt(s) component refers to any toxicologically harmless calcium salt at a pH where the calcium salt is capable of releasing more calcium ions than $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ at pH 7.0. In use, the solid products of
25 the present invention for the remineralization of enamel and/or dentin tubules release to the saliva in the local areas of application at least about 100 ppm, preferably, at least about 1000 ppm of calcium ions to the water and/or saliva, the upper limit is about 35,000 ppm of
30 calcium ions.

The anionic salt(s) of the solid products contains at least one water-soluble or partially water soluble phosphate salt in an amount such that the mixed

aqueous and/or saliva composition in the local area of application will contain dissolved phosphate anions. The mixed aqueous composition will preferably contain at least about 100 ppm, more preferably from about 500 ppm to about 40,000 ppm, of the dissolved phosphate anions. A portion of the phosphate salt may be present in the mixed aqueous composition as undissolved phosphate salt.

The term "water-soluble" as used herein with respect to the phosphate, fluoride and divalent metal salts suitable for use in the present invention refers to a solubility such that the salts are each capable of having a solubility in water of at least about 0.25 gm in 100 ml of water at about 20°C.

As stated previously herein, the products may further contain one or more non-toxic, water-soluble or partially water soluble salt of a divalent metal other than calcium. The solid product contains an amount of the divalent metal salt such that the mixed aqueous and/or saliva composition contains dissolved divalent metal cations. The presence of such dissolved divalent metal cations in the mixed aqueous composition may help to stabilize the composition in the local area of application against premature precipitation of the calcium cations and the phosphate anions to help in allowing the remineralizing cations and anions to diffuse through the tooth surface to the subsurface lesion(s) and/or exposed dentin tubule(s) prior to precipitating. As a result, when an effective amount of dissolved divalent metal cations is present in the mixed aqueous composition, the subsurface lesion is more effectively remineralized and/or the exposed dentin tubule(s) is more effectively mineralized when divalent metals other than calcium are added. The mixed aqueous composition in the

local areas of application may contain from about 100 ppm, more preferably from about 500 ppm to about 40,000 ppm, of the dissolved divalent metal cations.

The products may further contain at least one
5 water-soluble fluoride salt, the caries-prophylactic activity of which has long been established. However, because of the potential for fluorosis or other toxic effects, high levels of such fluoride salt(s) in the products are undesirable. Preferably, the total quantity
10 of fluoride applied is such as to limit ingestion and/or absorption of fluoride to no more than about 1 mg per use and preferably to less than about 0.1 mg. Low concentrations of fluoride anions can be useful in the mixed aqueous compositions in the local areas where the
15 products are applied. Such local low concentration levels of fluoride anions preferably range from about 1 ppm to about 2000 ppm.

Suitable fluoride salts for use in the present invention include the alkali fluorides such as sodium,
20 potassium, lithium or ammonium fluoride; tin fluoride; indium fluoride; zirconium fluoride; copper fluoride; nickel fluoride; palladium fluoride; fluorozirconates such as sodium, potassium or ammonium fluorozirconate or tin fluorozirconate; fluorosilicates; fluoroborates; and
25 fluorostannites. Organic fluorides, such as the known amine fluorides, are also suitable for use in the products of the present invention.

Water-soluble alkali metal monofluorophosphates such as sodium monofluorophosphate, lithium
30 monofluorophosphate and potassium monofluorophosphate, (the sodium monofluorophosphate being preferred) may be employed. In addition, other water-soluble

monofluorophosphate salts may be employed, including, for example, ammonium monofluorophosphate, aluminum monofluorophosphate, and the like.

5 The solid products of the present invention provide from about 0.01% to about 15.0%, preferably from about 0.10% to about 10.0%, by weight of the water-soluble or partially water soluble calcium salt. The solid products may further provide 0.001%, more preferably from about 0.0001% to about 2.0%, and most
10 preferably from about 0.01% to about 1.0%, by weight of the divalent metal salt(s) other than calcium as previously discussed herein.

The products of the present invention contain from about 0.01% to about 15.0%, preferably from about
15 0.10% to about 10.0%, by weight of the water-soluble or partially water soluble phosphate salt(s). The solid product may further contain up to about 5000 ppm, more preferably from about 1 to 1000 ppm of fluoride ion.

The products of the present invention contain a
20 molar ratio of the calcium salt(s) to the phosphate salt(s) of from about 0.01:1 to about 100:1. Preferably, the concentration of the calcium salt(s) and the concentration of the phosphate salt(s) are in the range of about 5:3 to about 1:1 in the products.

25 Any suitable water-soluble or partially water soluble calcium salt can be employed to practice the present invention. Preferred water-soluble calcium salts include, but are not limited to, calcium acetate, calcium lactate, calcium chloride, calcium gluconate, calcium
30 glycerophosphate, calcium nitrate, monocalcium orthophosphate, i.e., $\text{Ca}(\text{H}_2\text{PO}_4)_2 \cdot \text{H}_2\text{O}$ and the like.

Calcium salts which are normally insoluble at neutral or alkaline pHs can be used if an acidic component is present to increase solubility. Such water-insoluble calcium salts include, but are not limited to, calcium phosphate such as dicalcium phosphate, calcium hydroxyapatite and the like.

When such water-insoluble or partially water-soluble calcium salts are employed, acidic material may be added to the product to ensure the solubility of the calcium salts in the water and/or saliva. Any acid compound suitable for maintaining the solubility of calcium salts can be employed. Specific examples of such acid compounds are discussed below.

Calcium salts of partial water-solubility that can be used to practice the present invention include, but are not limited to, calcium sulfate, anhydrous calcium sulfate, calcium sulfate hemihydrate, calcium sulfate dihydrate, calcium malate, calcium tartrate, calcium malonate, calcium succinate, and mixtures of the foregoing. Calcium sulfate is the preferred partially water-soluble calcium salt.

As used herein, the term "partially water-soluble" with respect to the calcium salt component refers to any toxicologically harmless calcium salt having a solubility in water which is greater than that of dicalcium phosphate dihydrate in an aqueous solution having a pH of about 7.0 and a temperature of about 25°C but which is less than that solubility which would release more than about 1400 ppm of calcium cations in such aqueous solution. In an aqueous solution having a pH of about 7.0, dicalcium phosphate dihydrate generally releases about 40 ppm of calcium cations. Thus, the partially water-soluble calcium salt(s) used in the

present invention generally has a solubility in water such that the salt releases more than about 40 ppm but no more than about 1400 ppm of calcium cations in an aqueous solution having a pH of about 7.0 at a temperature of about 25°C. Preferably, the partially water-soluble calcium salt(s) used in this invention has a solubility in water such that the salt(s) releases from about 100 ppm to no more than about 1400 ppm of calcium in such aqueous solution.

In the present invention, the principle known as the "common ion effect" also can be used to control the solubility of the partially water-soluble calcium salt(s) used and to optimize calcium release and fluoride stability. To achieve the common ion effect, a water-soluble "common anion" salt can be added to the products wherein the anion of the salt is the same as the anion present in the calcium salt employed. In the present invention, the preferred "common anion" salts are the sodium, potassium and ammonium salts. However, an anion which is part of another functional ingredient may also be added. For example, the use of magnesium sulfate in a calcium sulfate-based formulation can supply at least some of the needed sulfate anion.

Any water-soluble inorganic orthophosphate salt(s) can be used to practice the present invention. Such orthophosphate salts include, but are not limited to, alkali salts and ammonium salts of orthophosphoric acid such as potassium, sodium or ammonium orthophosphate; monopotassium phosphate; dipotassium phosphate; tripotassium phosphate; monosodium phosphate; disodium phosphate and trisodium phosphate and the like. Such phosphate salts may provide for an acid buffer system to provide for a suitable pH to solubilize the

calcium and phosphate salts upon the release of the salts from the product into the water and/or the saliva. More alkaline phosphate salts can be employed to practice the present invention, however, such phosphate salts need to
5 be combined with acidic compounds to provide for an acidic environment to solubilize the calcium and phosphate salts released from the product into water and/or saliva.

In addition to water-soluble phosphate, the
10 solid products can also include partially water-soluble phosphate such as magnesium phosphate. The term "partially water-soluble" with respect to the partially water-soluble phosphate compound refers to a phosphate compound having a solubility such that in an aqueous
15 solution having a pH of about 7.0 and a temperature of about 25°C, the phosphate compound is capable of releasing more than about 40 ppm but no more than about 1400 ppm of phosphate anions, preferably from about 100 ppm to no more than about 1400 ppm of phosphate anions,
20 by weight of the aqueous solution.

Suitable pH-adjusting compounds, i.e., acids, bases or buffers, can be included in the products of the present invention to assure that the mixed aqueous compositions formed therefrom will have a pH within the
25 ranges mentioned above. The pH of the mixed aqueous composition in local areas where the product is applied may be controlled by adding to the product or the mixed aqueous composition any acid, base or buffer which is safe for use in the oral cavity and which yields the
30 desired pH at the amount used. Examples of suitable acids include acetic acid, phosphoric acid, citric acid, gluconic acid, tartaric acid, and malic acid. Suitable buffers which can be used include, but are not limited

to, e.g., sodium citrate, tartrate, lactate, benzoate, carbonate, bicarbonate, malate, disodium hydrogen phosphate, sodium dihydrogen phosphate and the like.

The divalent metal compound(s) which can be used in the products of the present invention may be any water-soluble, non-toxic divalent metal compound which will help stabilize the calcium, phosphate and fluoride ions such that these ions do not rapidly or prematurely precipitate before diffusing into the teeth. In practice, however, it has been found that at least one member selected from the group consisting of magnesium, strontium, tin, and zinc, with magnesium being preferred, is the most effective divalent metal in stabilizing the system.

Suitable magnesium compounds include, for example, magnesium acetate, magnesium ammonium sulfate, magnesium benzoate, magnesium bromide, magnesium borate, magnesium citrate, magnesium chloride, magnesium gluconate, magnesium glycerophosphate, magnesium hydroxide, magnesium iodide, magnesium oxide, magnesium propionate, magnesium D-lactate, magnesium DL-lactate, magnesium orthophosphate, magnesium phenolsulfonate, magnesium pyrophosphate, magnesium sulfate, magnesium nitrate, and magnesium tartrate. Preferred magnesium compounds are magnesium chloride, magnesium acetate and magnesium oxide.

Suitable strontium compounds include, for example, strontium acetate, strontium ammonium sulfate, strontium benzoate, strontium bromide, strontium borate, strontium caprylate, strontium carbonate, strontium citrate, strontium chloride, strontium gluconate, strontium glycerophosphate, strontium hydroxide, strontium iodide, strontium oxide, strontium propionate,

strontium D-lactate, strontium DL-lactate, strontium pyrophosphate, strontium sulfate, strontium nitrate, and strontium tartrate. Preferred strontium are strontium acetate, strontium chloride, strontium nitrate.

5 Suitable tin compounds include, for example, stannous acetate, stannous ammonium sulfate, stannous benzoate, stannous bromide, stannous borate, stannous carbonate, stannous citrate, stannous chloride, stannous gluconate, stannous
10 glycerophosphate, stannous hydroxide, stannous iodide, stannous oxide, stannous propionate, stannous D-lactate, stannous DL-lactate, stannous orthophosphate, stannous pyrophosphate, stannous sulfate, stannous nitrate, and stannous tartrate. A preferred tin compound is stannous
15 chloride.

 Suitable zinc compounds include, for example, zinc acetate, zinc ammonium sulfate, zinc benzoate, zinc bromide, zinc borate, zinc citrate, zinc chloride, zinc gluconate, zinc glycerophosphate, zinc
20 hydroxide, zinc iodide, zinc oxide, zinc propionate, zinc D-lactate, zinc DL-lactate, zinc pyrophosphate, zinc sulfate, zinc nitrate, and zinc tartrate. Preferred zinc compounds are zinc acetate, zinc chloride, zinc sulfate, and zinc nitrate.

25 If the cationic salt(s) is aqueous, the aqueous cationic salt may contain an amount of dissolved calcium cations released by the calcium salt and an amount of an undissolved form of the calcium salt. The aqueous cationic salt preferably contains no more than about
30 0.14% by weight, more preferably no more than about 0.08%, most preferably from about 0.01% to about 0.05%, by weight of dissolved calcium cations. In addition, the aqueous cationic component preferably contains at least

about 0.05%, more preferably at least about 0.20%, most preferably from about 0.20% to about 0.30%, by weight of the undissolved form of the calcium salt.

If the cationic component further contains at least one salt of a divalent metal other than calcium, as discussed previously herein, the aqueous cationic component may further contain dissolved divalent metal cations released by the divalent metal salt.

If the cationic component also contains a "common-anion" salt as previously described herein, the aqueous cationic component may further contain dissolved ions released by the common-anion salt.

If the anionic component is aqueous, the aqueous anionic component may contain dissolved phosphate anions released by the phosphate salt. If the anionic component further contains at least one water-soluble fluoride salt as previously discussed herein, the aqueous anionic component may further contain dissolved fluoride anions released by the fluoride salt.

Another embodiment of the product of the present invention is a water-soluble, dry-mix product capable of being combined with a non-aqueous solid carrier medium or with an aqueous liquid medium to form a remineralizing/mineralizing product. Such dry-mix product contains (a) from about 1.0% to about 80.0% by weight of the water-soluble calcium salt(s) and from about 1.0% to about 80.0% by weight of the water-soluble phosphate salt(s), and (b) from about 1.0% to about 80.0% by weight of the water-soluble alkaline salt(s). To prevent premature reaction between components (a) and (b), the components can be encapsulated as discussed below. However, if the materials are in an anhydrous form such materials need not be encapsulated. In

preferred embodiments, the dry mix product of the present invention further contains from about 0.1% to about 20.0% by weight of the divalent metal salt(s) discussed previously herein. In addition, the dry mix product may
5 also contain up to about 0.01% by weight of the fluoride salt(s) discussed hereinabove. The dry-mix product may be mixed with a solid carrier medium such as a water-soluble wax.

The carrier component of the solid products of
10 the present invention can be any suitable gum, starch, wax or polymeric material which can release the calcium and phosphate salts, preferably simultaneously, into the water and/or saliva and which also can be readily coated on a surface of a solid substrate of the solid product.

15 Examples of suitable gums and starches include, but are not limited to, gum acacia, gum arabic, gum tragacanth and the like; starches such as corn starch, dextrans and the like can be employed.

The preferred waxes for coating the solid
20 substrate are those that are white or colorless, are relatively soft and have a melting point of from about 140°F to about 300°F. Such waxes include, but are not limited to, beeswax, paraffin and microcrystalline waxes or mixtures thereof. Most preferred waxes are non-
25 hygroscopic but water soluble or easily water dispersable so as to prevent reaction of the salts prior to use, but which rapidly release the salts when applied. Such waxes include, but are not limited to polyethylene glycols such as those sold under the trademark "Carbowax" by Union
30 Carbide Corp., New York, and the like as well as mixtures thereof. Such most preferred waxes also include polyoxyethylene or polyoxypropylene or mixed block copolymers of ethylene oxide and propylene oxide.

Examples of such polymers are the "Plurionics" sold by BASF. An example of such "Plurionics" is Pluronic® F127. The wax comprises about 2% to about 30% by weight of the solid product, preferably about 10% to about 25% by weight.

For added appeal, the wax portion of the solid product can carry flavor oils spray dried into suitable water-soluble carriers. These flavors are then included in the wax during the manufacture of the solid product according to methods known to those familiar with the art. Upon use, the water present in the oral fluids releases the flavor.

The present invention also utilizes other polymeric materials than those described above as a carrier for the remineralization salts. Such polymeric coating materials preferably have good adhesion, clarity, toughness, and are non-toxic. Further, it is desirable that the polymeric material be a film former such that a uniform continuous coating on the substrate can be achieved. It is further desired that the polymeric material be capable of hydration whereby the film formed is water pervious allowing for rapid and simultaneous release of calcium and phosphate salts therefrom. Hydration means the mechanism by which the polymeric material absorbs and combines with water.

When such polymeric coatings are employed, it is preferable to first coat the substrate with a layer of wax to ensure adhesion of the polymer to the substrate. Good adhesion of the polymeric coating to the wax layer or coating of the substrate is important to ensure composition integrity such that the remineralization salts incorporated into the polymeric coating adhere to

the substrate. Clarity of the coating is desirable to allow dyes applied to the substrate to be visible, and thus allow more aesthetic flexibility.

The polymeric coating preferably is
5 sufficiently tough to resist abrasion of the substrate to prevent cracking or flaking and resultant loss of the remineralization salts before placement of the solid product in the oral cavity.

Specific polymeric coatings which are useful in
10 the present invention include, but are not limited to;

- a. alkyl monoesters of poly(methyl vinyl ether/maleic acid);
- b. polyvinyl pyrrolidones;
- c. acrylamide/acrylate/butylaminoethyl
15 methacrylate polymers. Polymers of this type are sold by National Starch & Chemical Corporation under the trademark "Amphomer";
- d. vinyl acetate/crotonic acid/vinyl
20 neodecanoate terpolymers. Terpolymers of this type are sold by National Starch & Chemical Corporation under the trademark "Resyn 28-2930";
- e. vinyl acetate/crotonic acid copolymers.
25 Copolymers of this type are sold by the National Starch & Chemical Corporation under the trademark "Resyn 28-1310";
- f. terpolyamides comprised of the
30 copolymerization products of three polyamide precursors, a dicarboxylic acid-diaamine reaction product and a lactam. Terpolymers of this type are sold by Belding Chemical Industries as the BCI-600

series nylons;

g. hydroxypropyl cellulose. Polymers of this type are sold by Hercules Incorporated under the trademark "Klucel".

5 The polymeric coating placed on the surface of the wax preferably comprises from about 1 to about 10 percent by weight of the final product. If the polymeric coating is less than about 1 percent of the product weight it may be ineffectual in keeping sufficient
10 calcium and phosphate salts adhered to a surface of the solid substrate. If it is more than about 10 percent of the product weight the coating may adversely affect product aesthetics.

 In addition to incorporating the calcium and
15 phosphate salts into a wax or polymer material, the salts can additionally be encapsulated in a separating component. Encapsulation within the context of the present invention means that the ion particles of the components can be entirely coated or only partially
20 coated. The ions are encapsulated such that the cationic and anionic salts are preferably released simultaneously into the water and/or saliva. In addition to providing a means of controlling the release of the cationic and anionic components of the product into water and/or
25 saliva, encapsulation of the components prevents reaction of the components with substances such as traces of water in or absorbed into the product during storage. Also, encapsulation prevents undesirable premature reaction between the cationic and anionic ions of the solid
30 product. Preferably, the encapsulant is edible or rinsable from the mouth.

Suitable encapsulating or coating materials include oleophilic and other materials such as conventional edible gums, polymers which exhibit proportion ranging from hydrophilic to hydrophobic (water-insoluble), resins, waxes and mineral oils. Preferred polymers for coating or encapsulating the salt particles are hydrophilic organic polymers and hydrophobic (water-insoluble) organic polymers and mixtures thereof.

Suitable hydrophilic polymers include water-soluble and water-dispersible organic polymers. A mixture of polymers can be used, and from about 5.0% to about 95.0% by weight of a water-insoluble polymer can be included with the hydrophilic polymer.

Suitable hydrophilic polymers for coating the salt particles include, e.g., gum arabic, gum karaya, gum tragacanth, guar gum, locust bean gum, xanthan gum, carrageenan, alginate salt, casein, dextran, pectin, agar, sorbitol, 2-hydroxyethyl starch, 2-aminoethyl starch, maltodextrin, amylopectin, 2-hydroxyethyl cellulose, methyl cellulose, carboxymethyl cellulose salt, cellulose sulfate salt, polyvinylpyrrolidone, polyethylene glycol, polypropylene glycol, polyethylene oxide, polyvinyl alcohol/acetate, and the like.

Polyvinyl acetate is an example of a water-insoluble polymer which can be included as an additional coating component to moderate the hydrophilicity of a hydrophilic polymer coating.

Suitable water-insoluble polymers in combination with one or more other components, for coating the salt particles in the present invention

include polyvinyl acetate, polyacrylamide, polyvinylchloride, polystyrene, polyethylene, polyurethane, and the like.

The polymer coating can be applied to the cations and anions of the components by conventional means such as pan coating, fluidized coating, centrifugal fluidized coating, and the like. The coating polymer is usually dissolved in a suitable solvent such as water, methanol, ethanol, acetone, tetrahydrofuran, ethyl acetate, dimethylformamide and the like, as appropriate for a selected polymer species. A coating polymer can also be applied in the form of an emulsion or suspension. After the coating medium is applied to the particles, the solvent medium is removed by evaporation, thereby forming a continuous film coating which encapsulates the discrete particles.

The film coating thickness on the surface of the encapsulated component preferably ranges from about 0.1 to about 20 microns. The film coating can contain one layer or multiple layers, and may constitute from about 0.5% to about 50.0% of the total dry weight of the coated particles.

To allow release of the components from the core matrix of the encapsulated particles when the solid product is introduced into an aqueous environment, the surface coating of water-insoluble polymer may contain from about 5.0% to about 30.0% by weight of a particulate water-extractable organic or inorganic filler, such as, e.g., sodium monosaccharide or disaccharide, sorbitol powder, mannitol, and the like.

The rate of release of the encapsulated particles under aqueous conditions can be controlled by the quantity and type of polymer coating on the particle surface.

5 Low molecular weight hydrophilic polymers will release the particle core matrix content at a relatively fast rate in the presence of moisture. High molecular weight polymers which are less hydrophilic will release at a relatively slow rate. Additional rate control is
10 obtained by using mixtures of polymer components of varied hydrophilicity.

 Polyethylene glycol or polyvinyl alcohol will release the particle core matrix at a relatively fast rate. Polyethylene oxide or partially hydrolyzed
15 polyvinyl acetate will release at a relatively slow rate. Polyvinylpyrrolidone will release the particle core matrix content at an immediate rate when the encapsulated particles incorporated into the solid product are applied to the teeth.

20 Examples of suitable oleophilic coatings or encapsulating materials include paraffin; mineral oil; edible oils such as peanut oil, coconut oil, palm oil, or safflower oil; oleophilic organic esters such as isopropyl siloxane myristate or isopropyl palmitate;
25 edible polysiloxanes; and the like. Encapsulating salts with a mixture of paraffin and waxes are also suitable.

 The use of mineral oil as the oleophilic coating material is particularly advantageous because mineral oil will help in removing undesired bacteria
30 during the course of treatment of the teeth with the mixed aqueous composition formed of the solid products.

The oleophilic coating should be thick enough that the coating will either readily dissolve, disperse, emulsify or disintegrate in water and/or saliva during chewing or sucking of the product to release the salts.

5 If a water-insoluble oleophilic coating, e.g. mineral oil, is used, the coating phase can be pre-emulsified with a non-ionic, non-aqueous surfactant such as a hydrophilic ethoxylated sorbitan monooleate, e.g.,
10 the material sold under the trademark Tween. In this manner, when the product is placed in water or saliva, the oleophilic coating is emulsified more readily than without the emulsification agent being present. Other similar surfactants can be used such as sodium lauryl sulfate and other non-ionic surfactants. It is important
15 that the encapsulant does not impede the release of the calcium cations and the phosphate anions to lead to an undesirable imbalance of cations and anions into the water and/or saliva.

 In another embodiment, the calcium and
20 phosphate salts can be adsorbed onto or absorbed into a material such that the salts are released from the material upon contacting the water and/or the saliva. Examples of such suitable materials include, but are not limited to, silica, starch such as corn starch, wheat
25 starch and potato starch and metal oxides such as titanium dioxide and alumina.

 To incorporate the calcium and phosphate salts into or onto the particle material, any suitable method in the art may be employed. One method is to make a
30 slurry of the components and spray them onto the particles and let the particles with the components dry.

One advantage to incorporating the cationic and anionic components onto or into such materials is to prevent premature reaction between the components during storage which would result in the formation of an insoluble salt.

5 In the methods of the present invention, the tooth (or teeth) are treated with the mixed aqueous composition formed from the products of the present invention as described above. The tooth is treated with the mixed aqueous composition for a period of time
10 sufficient to allow the cations and the anions of the product to diffuse to the subsurface and/or dentin where the ions then precipitate an insoluble compound onto the subsurface lesion(s) and/or in the exposed dentin tubule(s). In this way, the subsurface lesion(s) is
15 remineralized and/or the exposed dentin tubule(s) is mineralized.

The actual treatment time with products of the present invention, e.g. dental floss, may be brief. However, deposits of the calcium and phosphate salts on
20 the teeth can remain for an extended period of time especially in the interproximal areas of teeth and in plaque for extended treatment of teeth.

As stated previously herein, the ions which have diffused through the tooth surface form an insoluble
25 precipitate in the demineralized subsurface lesion(s) and/or on the exposed dentin tubule(s). Although many precipitates are within the broad scope of the present invention, it is preferred that the precipitate render the remineralized subsurface and/or mineralized dentin of
30 the tooth treated in accordance with the present invention more resistant to demineralization than was the original enamel. Thus, the preferred precipitate is one which is less soluble than the original enamel.

Tooth enamel primarily contains a slightly carbonated apatite. If the precipitating species is not carbonated, the precipitate will be somewhat less soluble than the original enamel. Therefore, when fluoride
5 anions are not present, it is desirable that conditions be present which favor the precipitation of unsubstituted hydroxyapatite. Thus, for example, it is desirable to avoid the addition of carbonates or bicarbonates to non-fluoride compositions. On the other hand, if fluoride
10 salts are used in the products of this invention, the apatite will incorporate fluoride anions, thus rendering the precipitate more resistant to demineralization than was the original enamel. However, even when fluoride anions are not directly added to the
15 remineralizing/mineralizing solid product used in the present invention, it has been found that the teeth treated with such composition will absorb more fluoride when subsequently treated with a fluoride-containing product (e.g., a fluoride toothpaste) than teeth which
20 have not been pretreated with such composition. Thus, the precipitate formed in the present invention is preferably a calcium phosphate or a hydroxyapatite.

Therefore, use of the products of the present invention not only remineralizes the demineralized enamel
25 and/or mineralizes the exposed dentin tubules but also renders such remineralized enamel and/or mineralized dentin tubule more resistant to subsequent demineralization than was the original enamel or tubule.

The mixed aqueous composition formed from the
30 products of the present invention and the insoluble precipitate formed from the mixed aqueous composition both have acceptable levels of toxicity. In other words, the particular ions, in the amounts used in the

remineralization and/or mineralization process, are non-toxic. Furthermore, such composition and precipitate preferably be otherwise compatible in the oral environment.

5 It has been found that even with the use of the divalent metal salt(s) and the acid compounds discussed previously herein and the presence of the solid, non-aqueous, carrier medium, some reaction between calcium cations, phosphate anions and, if present, fluoride
10 anions, may occur in the products of the present invention during storage thereof (for example, in a closed container or package). Such reaction results in the formation of an insoluble precipitate such as calcium phosphate. To avoid such a reaction, the present
15 invention includes embodiments of the solid products that contain a stabilizing agent which helps to prevent the calcium and phosphate ions (and fluoride ions, if present) from reacting. Such a stabilizing agent may be used in place of the divalent metal salt(s) or may be
20 used in addition to the divalent metal salt(s).

Suitable stabilizing agents for use include any orally acceptable material that can stabilize one or more of the calcium salt(s), phosphate salt(s) and/or fluoride salt(s) during storage of the product. Non-limiting
25 examples of such stabilizing agents include desiccating agents, coating or encapsulating materials, and mixtures of the foregoing.

Non-limiting examples of suitable desiccating agents include magnesium sulfate, sodium sulfate, calcium
30 sulfate, calcium chloride, and colloidal silica, e.g., colloidal silica particles centered together in chain-like formations having surface areas of from about 50 to about 400 square meters per gram such as materials sold

under the trademark Cab-O-Sil by Cabot Corporation. Such materials stabilize the products by, for example, absorbing any existing water either present in or contacted with the composition to prevent reaction of the calcium, phosphate and/or fluoride salts.

When used, the stabilizing agent is present in the products in an amount effective to inhibit reaction between the calcium, phosphate and/or fluoride salts during storage thereof, while allowing release of sufficient calcium, phosphate and/or fluoride ions when the product is contacted with water and/or saliva. The stabilizing agent is present in an amount of up to about 7.5% by weight, preferably from about 0.01% to about 5.0% by weight.

The solid substrate of the solid product can be any suitable water-insoluble material employed to make dental floss, dental tape, tooth picks dental adhesive, dental implants and the like.

Tooth picks are composed of wood, plastic, metal, ivory, bone and the like. Tooth picks come with single and double rounded ends. Tooth picks also come as flat and flat at one end and rounded at the other. Tooth picks within the scope of the present invention can be prepared by any method employed in the art.

The solid substrate of the present invention can also be any water-insoluble material suitable for dental floss, dental tape, dental adhesives, dental implants, and the like. It is to be understood that the term "dental floss" hereinafter encompasses dental tape as well as any similar article. The dental floss, or dental tape substrate comprises a plurality of individual filaments of a substance suitable for use as a dental floss, including, for example, nylon 6 and 66, rayon,

Dacron, acetate polymers, polypropylene and similar monofilament yarns as well as cotton, wool, and other staple yarns. The plurality of smaller fibers are combined together to form a yarn of larger size small
5 enough to pass between closely contacting teeth. If desired, the yarn filaments can be colored utilizing any suitable dye such as FD&C Blue No. 1, FD&C Yellow No. 10, FD&C Green No. 3, FD&C Red No. 40, or mixtures of these or other similar dyes.

10 The preferred means of combining the fibers is to twist them together to form a floss product more resistant to shredding and filament separation than would otherwise be achieved. Dental floss can be made with little or no twist or it can be braided as in a dental
15 tape. The twist can be from 0.0 to 6.0 turns per inch, with a preferred twist of 2.0 to 4.0 turns per inch.

The tensile strength of the finished floss should be between 5 and 25 pounds, although higher tensile strengths are acceptable. The preferred tensile
20 strength is about 7 to 15 pounds. A finished yarn of less than 5 pounds will tend to break easily during use and is unacceptable for a dental floss, and a finished yarn of more than 25 pounds tensile strength offers no advantages yet is less economical to manufacture. The
25 yarn may be of 200 to 2000 denier, while the preferred dental floss is of 500 to 1600 denier for proper hand feel.

Dental adhesives included within the scope of the present invention include adhesives which can be
30 coated on at least one surface with the gums, starches, polymers and waxes employed as separating components. The dental adhesives can be prepared by any suitable method employed in the art. The dental adhesive can be

composed of materials which include, but are not limited to, monofunctional methacrylates such as methacrylic acid, lower alkyl methacrylates (e.g., where the alkyl group has 1 to 4 carbon atoms such as methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec.-butyl and tert.-butyl),
5 tetrahydrofurfuryl methacrylate and glycidyl methacrylate. Other methacrylate monomers include polyfunctional methacrylates which have two or more methacrylate moieties per molecule.

10 Dental implants which can be employed to practice the present invention include, but are not limited to ceramic materials. Such ceramic materials may include monocrystalline alumina ceramics, polycrystalline alumina ceramics, zirconium dioxide ceramics and the
15 like.

The water-soluble substrate of the present invention can be coated with the separating component containing the remineralization salts by any suitable method used to coat a solid substrate. Such methods may
20 include spray coating or pan coating and the like.

The following Example is intended to further illustrate the present invention but is not intended to limit the scope of the invention.

Example

25 A nylon 6 filament is passed through a bath of melted bees wax followed by passing the nylon 6 through a chamber of refrigerated air to effect solidification of the wax. Alternatively, the coating may also be applied by passing the nylon 6 filament through a bath of the wax
30 in solution using a suitable solvent, such as methylene chloride. After coating, the solvent is flashed off using radiant heater or high velocity hot air. If a dye

and/or a flavor is to be included, the same is placed into the wax bath or solution and thus it is coated onto the filament along with the wax.

Once the wax layer is applied to the dental floss substrate or filaments, the polymeric coating and calcium and phosphate salts may be applied in a number of ways. The wax-coated nylon 6 filament may pass through a solution of the polymeric coating in a volatile solvent and then, before the solvent is flashed off, the calcium and phosphate salts are dusted onto the wet floss. Once coated, the floss is passed through an oven or drying chamber to flash off the solvent.

Alternatively, the solvent-wet floss, having been coated with the polymeric material, is passed through the calcium and phosphate salt powders such that the tacky surface of the floss picks up the salts and helps them adhere to the surface. The floss is then passed through an oven or drying chamber to flash off the solvent.

Still another method of adding the calcium and phosphate salts to the floss is by spraying the wet floss with the powders as the floss is wound on the rewind supply spool just after the coating is applied. This may cause some of the particles to be impregnated more firmly into the polymeric coating due to mechanical compression.

Still another method of impregnating the floss with calcium and phosphate salts is the inclusion of the calcium and phosphate salts in the polymeric material solution tank. Since the salt particles tend to settle out in the tank, the slurry formed by the particles in the solution preferably are subjected to sufficient mixing to keep the particles in suspension. A homogeneous suspension is required to make the level of

remineralization salts as uniformly distributed along the floss as possible. The floss is then passed through the slurry of coating and remineralization salts by means of guides or wheels. The floss thus coated with a layer of the wet slurry then is dried by standard means such as passing through an oven or drying chamber to flash off the solvent.

Dental floss in accordance with the present invention exhibits a desirable surface texture. It provides excellent cleaning to the interproximal surfaces of the teeth, while delivering an effective amount of calcium and phosphate salts to the teeth of the user to remineralize the teeth and to combat dental caries.

In addition to the embodiments described herein, other arrangements and variations within the scope and spirit of the invention will occur to those skilled in the art.

WHAT IS CLAIMED IS:

1. A solid product for remineralizing subsurface lesions and/or for mineralizing exposed dentin tubules in teeth, comprising:
 - 5 (a) a cationic component of at least one calcium salt;
 - (b) an anionic component of at least one phosphate salt;
 - (c) a carrier component for retaining
 - 10 components (a) and (b) in the product such that the components do not react in the product prematurely; and
 - (d) a water-insoluble, solid substrate to which components (a), (b) and (c) adhere to a surface of the solid substrate; the solid product being capable of
 - 15 simultaneously releasing the components (a) and (b) into water and/or saliva when the solid product is contacted or mixed with the water and/or saliva.
2. The product of claim 1, wherein the components (a) and (b) form a mixed aqueous composition
- 20 with the water and/or saliva such that the mixed aqueous compositions has a pH of from about 4.0 to about 10.0.
3. The solid product of claim 1, wherein the cationic component comprises from about 0.01 wt.% to about 15.0 wt.% of the at least one calcium salt.
- 25 4. The product of claim 1, wherein the anionic component comprises from about 0.01 wt.% to about 15.0 wt.% of at least one phosphate salt.
5. The solid product of claim 1, wherein the calcium salt of the cationic component comprises a water-
- 30 insoluble calcium salt, a water soluble calcium salt or a partially water-soluble calcium salt or mixtures thereof.

6. The product of claim 5, wherein the water-soluble calcium salt comprises calcium acetate, calcium lactate, calcium chloride, calcium gluconate, calcium glycerophosphate, calcium nitrate, or monocalcium orthophosphate.

7. The product of claim 1, wherein the at least one phosphate salt comprises a water-soluble phosphate salt, a partially water-soluble phosphate salt or mixtures thereof.

8. The product of claim 7, wherein the water-soluble phosphate salt comprises alkali salts of orthophosphoric acid or mixtures thereof.

9. The product of claim 1, wherein the cationic component further comprises at least one non-toxic, salt of a divalent metal other than calcium in an amount such that the water and/or saliva further comprises dissolved divalent metal cations.

10. The product of claim 9, wherein the divalent metal is a stabilizing agent.

11. The product of claim 10, wherein the divalent metal comprises magnesium, tin, strontium or zinc.

12. The product of claim 1, wherein the carrier component of the solid product further comprises malic acid, gluconic acid, tartaric acid, acetic acid, phosphoric acid, citric acid and the like.

13. The product of claim 1, wherein the anionic component further comprises fluoride anions.

14. The product of claim 1, further comprising an encapsulating coating disposed on one or both of the cationic and anionic components, the encapsulating coating readily dissolving, dispersing or emulsifying in the water and/or the saliva.

15. The product of claim 1, wherein the solid substrate is composed of nylon, rayon, Dacron, acetate, cotton, wool, polyester, polypropylene, wood, methacrylate, ceramic material and the like.

5 16. The product of claim 1, wherein the carrier component (c) is a wax comprising beeswax, paraffin, microcrystalline waxes, polyethylene glycols, polyoxyethylene, polyoxypropylene, mixed block copolymers of ethylene oxide and propylene oxide or mixtures
10 thereof.

17. The product of claim 16, further comprising a polymeric coating over the wax, the polymeric coating selected from the group consisting of:

15 alkyl monoesters of poly(methyl vinyl ether/maleic acid);

polyvinyl pyrrolidones;
acrylamide/acrylates/butyl/aminoethyl/methacrylate polymers;

20 vinyl acetate/crotonic acid copolymers;
vinyl acetate/crotonic acid/vinyl neodecanoate terpolymers;

terpolyamides comprised of copolymerization products of three polyamide precursors, a dicarboxylic acid-diamine reaction product, a second but dissimilar
25 dicarboxylic acid-diamine reaction product and a lactam; and hydroxypropyl cellulose.

18. The product of claim 16, wherein the wax comprises from about 2 to about 30 wt.% of the solid product.

30 19. The product of claim 17, wherein the polymeric coating comprises from about 1 to about 10 wt.% of the solid product.

20. The product of claim 1, wherein the carrier component (c) comprises water-soluble matrix material comprising gum acacia, gum arabic, gum tragacanth, corn starch, dextrans and the like.

5 21. The product of claim 1, wherein the insoluble, solid substrate comprises dental floss, tooth picks, dental tape, a dental adhesive or a dental implant.

10 22. A method of remineralizing at least one lesion formed in a subsurface of at least one tooth and/or mineralizing at least one exposed tubule in a dentin portion of at least one tooth, comprising the steps of:

15 (1) providing a solid product comprising:
(a) a cationic component comprising at least one calcium salt;

(b) an anionic component comprising at least one phosphate salt;

20 (c) a carrier component for retaining the components (a) and (b) in the solid product such that components (a) and (b) do not react prematurely in the carrier; and

25 (d) a water-insoluble, solid substrate to which components (a), (b) and (c) adhere to a surface of the solid substrate; the solid product being capable of simultaneously releasing the components (a) and (b) into water and/or saliva when the product is contacted or mixed with the water and/or the saliva;

30 (2) contacting or mixing the components (a), (b) and (c) of the solid product with the water and/or saliva to form a mixed aqueous composition; and

(3) applying the mixed aqueous composition to the subsurface and/or to the dentin portion such that the calcium cations and phosphate anions form a water-insoluble precipitate in the subsurface and/or on the
5 dentin portion of the tooth.

23. The method of claim 22, wherein the mixed aqueous composition formed by contacting or mixing the components (a), (b) and (c) with the water and/or saliva has a pH of from about 4.0 to about 10.0.

10 24. The method of claim 22, wherein the cationic component comprises from about 0.01 wt.% to about 15.0 wt.% of the at least one calcium salt.

25. The method of claim 22, wherein the anionic component comprises from about 0.01 wt.% to about
15 15.0 wt.% of the at least one phosphate salt.

26. The method of claim 22, wherein the cationic component comprises water-soluble calcium salts, water-insoluble calcium salts or partially water-soluble calcium salts or mixtures thereof.

20 27. The method of claim 26, wherein the water-soluble calcium salt comprises calcium acetate, calcium lactate, calcium chloride, calcium gluconate, calcium glycerophosphate, calcium nitrate, or monocalcium orthophosphate.

25 28. The method of claim 22, wherein the at least one phosphate salt comprises a water-soluble phosphate salt, a partially water-soluble phosphate salt or mixtures thereof.

30 29. The method of claim 28, wherein the water-soluble phosphate salt comprises alkali salts of orthophosphoric acid, ammonium salts of orthophosphoric acid or mixtures thereof.

30. The method of claim 22, wherein the cationic component further comprises at least one non-toxic, salt of a divalent metal other than calcium in an amount such that the water and/or saliva further
5 comprises dissolved divalent metal cations.

31. The method of claim 30, wherein the divalent metal cation is a stabilizing agent.

32. The method of claim 31, wherein the divalent metal comprises magnesium, tin, strontium or
10 zinc.

33. The method of claim 22, wherein the carrier component of the solid product further comprises malic acid, gluconic acid, tartaric acid, acetic acid, phosphoric acid, citric acid and the like.

15 34. The method of claim 22, wherein the anionic component further comprises fluoride anions.

35. The method of claim 22, further comprising an encapsulating coating disposed on one or both of the cationic and anionic components, the encapsulating
20 coating readily dissolving, dispersing or emulsifying in the water and/or the saliva.

36. The method of claim 22, wherein the solid substrate is composed of nylon, rayon, Dacron, acetate, cotton, wool, polyester, polypropylene, wood,
25 methacrylate, metal and the like.

37. The method of claim 22, wherein the carrier component is a wax comprising beeswax, paraffin, a microcrystalline wax, polyethylene glycols, polyoxyethylene, polyoxypropylene, mixed block copolymers
30 of ethylene oxide and propylene oxide or mixtures thereof.

38. The method of claim 37, further comprising a polymeric coating as a carrier component (c) coating the wax, the polymeric coating selected from the group consisting of:

5 alkyl monoesters of poly(methyl vinyl ether/maleic acid);

 polyvinyl pyrrolidones;
acrylamide/acrylates/butyl/aminoethyl/methacrylate
polymers;

10 vinyl acetate/crotonic acid copolymers;
 vinyl acetate/crotonic acid/vinyl neodecanoate
terpolymers;

 terpolyamides comprised of copolymerization
products of three polyamide precursors, a dicarboxylic
15 acid-diamine reaction product, a second but dissimilar
dicarboxylic acid-diamine reaction product and a lactam;
and hydroxypropyl cellulose.

39. The method of claim 37, wherein the wax
comprises from about 2 to about 30 wt.% of the solid
20 product.

40. The method of claim 38, wherein the
polymeric coating comprises from about 1 to about 10 wt.%
of the solid product.

41. The method of claim 22, wherein the
25 carrier component comprises water-soluble matrix material
comprising gum acacia, gum arabic, gum tragacanth, corn
starch, dextrans and the like.

42. The method of claim 22, wherein the
insoluble, solid substrate comprises dental floss, tooth
30 picks, dental tape, a dental adhesive, or a dental
implant.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/24529**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) : A 61 K 7/16, 7/18

US CL : 424/49 424/52

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/49 424/52

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,209,251 A (CURTIS et al.) 11 May 1993, (see claim 9, mixtures of water soluble calcium salts and water soluble phosphate salts in wax coated dental floss).	1-42
X	US 4,083,955 A (GRABENSTETTER et al.) 11 April 1978, (solid multi-layer lozenge toothpowder or chewing gum), see entire document.	1-20, 22-41
X	US 4,397,837 A (RAAF et al.) 09 August 1983, (solid two layer bon-bon or chewing gum), see entire document.	1-20, 22-41
X	US 5,336,264 A (CONSTANZ et al.) 09 August 1994, (dry bone cement pre-mix for teeth repair), see entire document.	1-20, 22-41

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*A* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

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Date of mailing of the international search report

12 APR 1999

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/24529

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,460,803 A (TUNG) 24 October 1995, (chewing gum or solid powders), see entire document.	1-20, 22-41
X	US 5,571,502 A (WINSTON et al.) 05 November 1996, (dry non-aqueous mix), see entire document.	1-20, 22-41
X	US 5,614,175 A (WINSTON et al.) 25 March 1997, (claims 13 - powder, granule, flake or tablet)1-20, 22-41	
X	US 5,645,853 A (WINSTON et al.) 08 July 1997, (solid chewing gum), see entire document.	1-20, 22-41

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